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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,430	01/07/2002	Gerald R. Crabtree	APBI-P05-008	4837
28120	7590	10/28/2003	EXAMINER	
ROPES & GRAY LLP			MYERS, CARLA J	
ONE INTERNATIONAL PLACE			ART UNIT	
BOSTON, MA 02110-2624			PAPER NUMBER	

1634

DATE MAILED: 10/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,430	CRABTREE ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 22-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Election/Restrictions

1. Applicant's election of group I, claims 1-21 in the response of June 18, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Information Disclosure Statement

2. In the information disclosure statement, the citations AJ, AK, AL and AM have been crossed off because U.S. applications are not appropriately listed in information disclosure statements. However, these applications have been considered by the Examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods for identifying immunosuppressive and immunostimulatory agents wherein the methods require the use of a NF-AT_C polypeptide. The specification discloses a single nucleic acid consisting of SEQ ID NO:

45 which encodes for a cytoplasmic component of the NF-AT complex, wherein the cytoplasmic polypeptide has the sequence of SEQ ID NO: 46. The specification (page 19) broadly defines an NF-AT_C polypeptide as including analogs and portions of NF-AT_C which have at least 25 amino acids that are substantially identical to a portion of SEQ ID NO: 46. The specification (page 19) also defines the phrase "substantial identity" as including sequences which share at least 85% identity over at least 20 nucleotide positions. The NF-AT_C polypeptide analogs are further defined in terms of being capable of binding to any degree to "other NF-AT_n" polypeptides and having the ability to localize to the nucleus upon T cell activation. The specification at page 19 states that these NF-AT_C polypeptides may lack biological activity. Accordingly, the claims as written encompass a huge genus of polypeptides having functional activities distinct from the polypeptide of SEQ ID NO: 46, yet the specification discloses only a single NF-AT_C polypeptide whose translocation and binding to NF-AT DNA binding sequences is correlated with an immune response. In view of the teachings in the specification, the broadest reasonable interpretation of the claims indicates that the claims are inclusive of homologs and allelic and mutant variants of the polypeptide of SEQ ID NO: 46 having the functional activities of binding to NF-AT_n and of being inducible in T cells and HeLa cells. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of

35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only 1 member of the broadly claimed genus of NF-AT_c polypeptides have been defined by their structure. The specification does not disclose any allelic variants or mutants of the NF-AT_c polypeptide of SEQ ID NO: 46. Further, the specification teaches only the human NF-AT_c polypeptide but does not teach any non-human homologs. No common structural feature characteristic of NF-AT homologs and variants has been described in the specification. It is noted that claims 1-19 do not provide any structural information for the claimed NF-AT_c polypeptide. Claim 20 defines the NF-AT_c polypeptide as comprising at least 25 amino acids which are substantially identical to SEQ ID NO: 46. Thereby, claim 20 is inclusive of methods of using a NF-AT_c polypeptide in which only

25 of the amino acids of the complete polypeptide have been defined and the defined amino acids broadly include amino acids having 85% identity with SEQ ID NO: 46. The specification has not exemplified any polypeptide fragments of 25 amino acids which are translocated across the nuclear membrane and/or which are phosphorylated and/or which have immunomodulatory activity and thereby could be used in a method for identifying an immune regulating agent. With respect to claim 21, the NF-AT_c polypeptide is defined in terms of hybridizing to a nucleic acid having the sequence of SEQ ID NO: 45 or the complement thereof. The claim does not set forth the conditions of hybridization and thereby includes polypeptides encoded by polynucleotides which cross-hybridize with SEQ ID 45 and which share minimal sequence complementary with SEQ ID NO: 45. The claim also includes polypeptides encoded by fragments of SEQ ID NO: 45. However, again, the specification has not adequately described a representative number of the allelic variants, mutants, homologs and fragments of polypeptides encompassed by the claims. Accordingly, while at the time of filing applicants were in possession of NF-AT_c polypeptides comprising SEQ ID NO: 46, the limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of a representative number of the broadly claimed NF-AT_c polypeptides and thus the written description requirement has not been satisfied for the claims as they are broadly written.

Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

4. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are indefinite over the recitation of "the test compound" because this phrase lacks proper antecedent basis. While the claims previously refer to a "test agent" and to a compound, the claims do not previously refer to a "test compound". Furthermore, claim 8 is indefinite over the recitation of "the compound" because it is not clear as to whether this refers to the compound of step (ii) or the test compound.

Claims 4 and 5 are indefinite over the recitation of "determining the binding of NF-AT to an NF-AT DNA binding sequence". The claims previously refer to only an NF-AT_C protein and do not refer generally to "NF-AT". It is therefore unclear as to whether the claims are intended to be limited to methods which detect binding of NF-AT_C or binding of the NF-AT complex. In the later case, the claims should be amended to clarify the relationship between NF-AT_C and NF-AT.

Claim 5 is indefinite over the recitation of "using a gel mobility shift assay". It is not clear as to how this limitation relates to the remainder of the claim and it is unclear as to whether the claim is intended to include an active process step of performing a gel mobility shift assay. This rejection may be overcome by amendment of the claim to recite, for example, "wherein determining the binding of NF-AT to a NF-AT binding sequence is performed using a gel mobility shift assay".

Claim 6 is indefinite over the recitation of "determining the level of expression..." because it is unclear as to how this phrase further limits the claim. It is unclear as to

whether the determining step is performed in addition to the step of assaying for nuclear translocation or whether the determining step constitutes a means for assaying for nuclear translocation.

Claims 9-16 are indefinite over the recitation of "NF-AT complex", "NF-AT binding sequence" and "NF-AT regulated enhancer region". While the claim previously refers to NF-AT_C and NF-AT_n, the claim does not clarify what constitutes "NF-AT" or the relationship between NF-AT_C or NF-AT_n and "NF-AT".

Claims 17 and 18 are indefinite over the recitation of "the test agent" because this phrase lacks proper antecedent basis. While the claims previously refer to a test compound, the claims do not previously refer to a test agent.

Claims 19-21 are indefinite over the recitation of "the NF-AT_C polypeptide" because this phrase lacks proper antecedent basis. While the claims previously refer to NF-AT_C, the claims do not previously refer to a "NF-AT_C polypeptide". Furthermore, claims 20 and 21 are indefinite over the recitation of "the NF-AT_C polypeptide or portion thereof" because the claims do not previously refer to portions of the NF-AT_C polypeptide.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,352,830. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '830 are both inclusive of methods for identifying immunosuppressive or immunostimulatory compounds wherein the methods comprise assaying for a compounds ability to alter nuclear translocation of NF-AT_C or assaying for compounds which alter the binding of NF-AT_C to NF-AT_n or compounds which alter phosphorylation of NF-AT_C.

6. Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-78 of U.S. Patent No. 6,150,099. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '099 are both inclusive of methods for identifying immunosuppressive or immunostimulatory compounds wherein the methods comprise assaying for a compounds ability to alter nuclear translocation of NF-AT_C or assaying for compounds which alter the binding of NF-AT_C to NF-AT_n or compounds which alter phosphorylation of NF-AT_C. The method steps of the presently claimed invention are the same as those set forth in the claims of '099 and the claims of

'099 generically screen for any compound that modulates the activity NF-AT which is inclusive of compounds that are immune regulating.

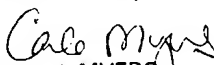
7. Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-90 of U.S. Patent No. 6,171,781. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '781 are both inclusive of methods for identifying immunosuppressive or immunostimulatory compounds wherein the methods comprise assaying for a compounds ability to alter nuclear translocation of NF-AT_C or assaying for compounds which alter the binding of NF-AT_C to NF-AT_n or compounds which alter phosphorylation of NF-AT_C. The method steps of the presently claimed invention are the same as those set forth in the claims of '781 and the claims of '781 generically screen for any compound that modulates the activity NF-AT (i.e., compounds that modulate the translocation or phosphorylation or binding activity of NF-AT). The genus of compounds to be screened in the methods of '781 is inclusive of compounds that are immune regulating.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
October 15, 2003


CARLA J. MYERS
PRIMARY EXAMINER